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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/044,423	CHOU, TZE-BIN	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *29-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in the response filed October 14, 2003 is acknowledged. The traversal is based on the following ground(s):

1. That the Examiner has failed to adequately show an undue search burden regarding the restriction of the methods indicated as Groups I and II, especially in light of the identical classification of these groups.

2. That the Examiner has failed to adequately show that the chromosomes indicated as Groups III and IV can be made by an alternative method from Groups I and II, such as "direct cloning."

Applicant's arguments ARE persuasive regarding the rejoinder of Groups I and II, but ARE NOT persuasive regarding the rejoinder of Groups III and IV along with Groups I and II. Applicant's arguments are not found persuasive because, as indicated in the MPEP, it is unnecessary for the Examiner to document the use of different products or processes, therefore the Examiner need not support that the chromosomes indicated in Groups III and IV can be made by an alternative mechanism. Furthermore, Applicant has not provided any evidence that the chromosomes *cannot* be made by an alternative mechanism, or refuted the Examiner's assertion in any factual manner. Furthermore, the methods of Groups I and II are patentably distinct from the chromosomes of Groups III and IV as evidenced by their distinct classifications, and their ability to be made by different methods.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-34 are pending in the instant application. Claims 29-34 have been withdrawn as being drawn to a non-elected invention. Claims 1-28 are under consideration in the instant application, and an Office Action on the merits is set forth below regarding these claims.

Information Disclosure Statement

The information disclosure statement filed December 12, 2002 has been considered, and a signed and initialed copy of the form PTO-1449 has been attached to this Office Action.

Specification

A substitute specification excluding the claims is required pursuant to 37 CFR 1.125(a) because the specification is not in the proper English vernacular. A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and (c).

Examples of how the instant specification is not in the proper English vernacular are set forth below. Applicant is reminded that these are only examples, and that the specification is replete with grammatical errors.

On page 1, paragraph [0002]:

"However, due to the systematic limitation, the possible living mechanisms are understood mostly through animal models which are composed by manipulated genes."

"The biological mechanism of Drosophila *Melanogaster* has the feature of evolutional conservation."

On page 2, paragraph [0003]:

"In the present time, as the structure genomic projects in model organisms are completed, how to decipher the flood of raw DNA sequences data in understanding gene function in vivo will be one of the major tasks for biology-related researchers."

The disclosure is further objected to because of the following informalities: the specification is not in sequence compliance. Although Applicant has submitted a preliminary amendment to indicate the SEQ ID NOS of sequences on pages 18 and 19 and Figures 1 and 4, Applicant has not indicated the proper SEQ ID NOS for the sequences on pages 21 and 22. Should these sequences not be represented in the Sequence Listing submitted previously by Applicant, Applicant must submit a new sequence listing (Paper and computer readable formats), and comply with CRF 37 § 1.821-1.825. It is noted that the non-compliance of the specification with the requirements of 37 CFR § 1.821-1.825 does not preclude the examination of the application. However, any response that fails to completely address these requirements will be considered Non-Responsive, and failure to address these issues may result in the Abandonment of the case.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15-20 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. Claim 15 indicates that the method is to be used for further experimentation. Further experimentation on the invention to further characterize the invention is not a patentable utility. Also, see the rejections under 35 USC § 112, first paragraph.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based

upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a method for making a clipped Drosophila chromosome (cFRT) that is insensitive to a *P* transposase, but remains sensitive to FLP recombinase. Claims 15-20, specifically, recite the limitation of "further experimentation" (see rejection under 35 USC § 101), therefore the nature of the invention also includes further experimentation.

State of the art. The state of the art is silent regarding the ability to make a clipped Drosophila chromosome that is insensitive to a *P* transposase, but remains sensitive to FLP recombinase. Therefore, the skilled artisan would be forced to rely on the instant specification in order to make and use the claimed invention.

Number of working examples and Guidance provided by applicant. The guidance and working examples set forth in the instant specification are equivalent to the language set forth in the claims. There are many method steps that recite indefinite limitations (see rejections under 112, second paragraph), where it is unclear what is to be performed in order to generate the cFRT. Because it is unclear what steps are to be taken in practicing the method, the skilled artisan cannot make or use the claimed method by relying on the instant specification.

Unpredictability of the art and Amount of experimentation required. The art is highly unpredictable because it is unclear what steps should be performed, what "further examinations" should be performed, etc., in order to practice the method. Because the

skilled artisan cannot ascertain this information from either the instant specification or the prior art, the skilled artisan would have to empirically determine these steps, resulting in an undue and unpredictable amount of trial and error experimentation. In fact, a limitation in claims 15-20 indicates that further experimentation is a required method step. As a result, the skilled artisan cannot make and use the claimed invention, thus the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are generally indefinite, reciting method steps that are unclear in what is to be performed in order to accomplish the step, or the method as a whole. Each issue of indefiniteness is addressed separately below.

Claims 1 and 22 are indefinite because it is unclear if the term "remaining functional to a yeast site-specific flippase recombinase" means that the chromosome encodes a function recombinase, or if it is "sensitive" to enzymatic action by the recombinase (in the same sense that it is insensitive to the *P* transposase). It would be remedial to exchange the term "functional" with "sensitive." Also, see step (d) of the same claims.

Claims 1 and 22 contain the limitation "exposing a *FRT* chromosome to said *P* transposase for occurring a local and imprecise transposition" in step (a) of the claimed methods. This limitation is indefinite because it is unclear if there is antecedent basis for

the term "said *P* transposase for occurring a local and imprecise transposition;" this is because it is unclear if the "occurring a local and imprecise transposition" is a characteristic of the transposase, or if it is a separate process step. In addition, it appears as if the term "causing" should replace the term "occurring" in order to bring the case into proper grammatical standing. If "occurring a local and imprecise transposition" is a process step, it would be remedial to indicate "(a) causing a local and imprecise transposition by exposing an FRT chromosome to said P transposase," etc. If it is a characteristic, there is no antecedent basis for the characteristic.

Claims 1, 22, 24 and 25 contain the limitation "screening said *P[FRT]* insertion insensitive to said *P* transposase to obtain screened products," which is indefinite because it is unclear what the screening step involves. One might assume that the screening step requires either the presence or the absence the selection marker gene contained in the *P[FRT]* insertion, but it is unknown which (if any) is required in the method. Additionally, it is not even clear if the selection marker is involved in the screening step, the selecting step (i.e., step (c)), neither or both. This further complicates step (c) of the method because it is unclear what is necessary to select "candidate products from said screened products."

Claims 1, 6 and 22 contain the limitation "selecting candidate products from said screened products by further examinations," which is indefinite because it is unclear what process is done (i.e., what are the further examinations) to distinguish candidate products from screened products. In other words, the selection process that is performed in order to arrive at a candidate product while eliminating screened products that are not adequate is unclear, therefore the method step is indefinite. This is because one of skill cannot

determine what "further examinations" will discern a "candidate product" from a "screened product."

Claims 1 and 22 contain the limitation "exposing said candidate products...and selecting a desired product by said further examinations," which is indefinite because: (a) it is unclear what the candidate product is being exposed to; and (b) it is unclear what a desired product is because it is still unclear what "further examinations" are performed to determine the desirability. The claim is indefinite as it relates to point (a) because the skilled artisan cannot expose the candidate product to an unknown element. The claim is indefinite as it regards point (b) because one cannot determine the "desirability" of a product (which is a relative term) if one does not know what criteria (i.e., the further examinations) are being used to definitively determine when a product is desirable.

Claim 2 recites the limitation "said clipped insertion" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. It is indefinite because the skilled artisan cannot determine if the cFRT or the *P[FRT]* insertion is what is examined.

Claims 3, 5 and 26 recite a limitation for examining the "homozygous viability" of a "screened product." This is indefinite because it is unclear how to screen the viability of a non-living biological molecule (i.e., the cFRT). Furthermore, it is unclear how this homozygous viability could in anyway represent a genetic background, as recited in claim 5.

Claim 5 recites the limitation "said chromosome's" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. It is unclear if the claim is referring to the cFRT or the *FRT* chromosome prior to clipping. It would

be remedial to indicate, "said *Drosophila* clipped FRT" or "cFRT" if the former is accurate.

Claim 8 is indefinite because it is unclear if the target sequence is recognized by the *P* transposase, or if it is mutated in such a manner that it is no longer recognized by the *P* transposase. Additionally in claim 8, the following grammatical issues require action: (a) the word "alternated" in line 3 should properly be "altered;" (b) the term "missing of" in sections (1), (2) and (3) is confusing- an alternative is to change it to "a sequence that is missing a..."

Claim 8 is indefinite for the recitation of the phrase "(3) missing of DNA sequences other than those defined in item (1) or item (2)." This skilled artisan cannot know what sequences are included or excluded from this group of sequences, therefore the claim is indefinite for not establishing the metes and bounds of the limitation.

Claim 9 is indefinite because of the phrase "remains the functional activity" in line 2 of the claim. It is unclear if the chromosome represents a functional activity, if the chromosome has a functional activity that it retains, or if it retains the ability to be acted upon in a functional manner.

Claim 10 recites the limitation "derived modification systems thereof," which is indefinite because it is unclear what derivation steps are required to arrive at such a modification system. As such, the skilled artisan cannot reasonably ascertain if a "derived modification system" is being used in the claimed method.

The term "effectiveness" in claims 10 and 11 is a relative term which renders the claim indefinite. The term "effectiveness" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill

in the art would not be reasonably apprised of the scope of the invention. The skilled artisan cannot reasonably ascertain how to practice the method because the skilled artisan cannot know what is being measured (i.e., what qualifications makes a cFRT effective), or what level of that measurement qualifies as "effective."

Claim 11 recites the phrase "for the description of said cFRT DNA sequences configuration." It is unclear what this term means in the context of the claimed method for generating a *Drosophila* clipped cFRT chromosome that is insensitive to a *P* transposase but remains sensitive to Flp.

Claim 12 recites the phrase "remains to behave normally as a wildtype chromosome feasible of various genetic manipulations." It is unclear what this phrase means, as it does not appear to be in the English vernacular. As such, one cannot reasonably be apprised of what the claim encompasses, therefore it is indefinite because the metes and bounds of the claim have not been defined.

Claim 13 is indefinite because it is unclear how a mutagen or an X-ray can cause the physical movement of a *P[FRT]* from a cFRT chromosome to a different chromosome, and what bearing this has on a method of making the cFRT chromosome.

Claims 13 and 14 recite the term "alternatively," but provide no alternatives. Claim 1, from which the claims depend, is directed to a method of making a chromosome. The terminology set forth in the instant claims suggests that, instead of making the chromosome (as set forth in claim 1), one should "alternatively" do something else instead of performing the elected claimed method (i.e., move an insertion or establish a cell line). Thus, the skilled artisan would not know if the method steps in

claim 1 were necessary perform the methods of claims 13 and 14, therefore the metes and bounds of the claim are not established.

Claims 15-20 is indefinite because it is unclear where the mutations are generated-in the selection marker, in the FLP sequences, in the *P* transposase sequences, etc. As such, the skilled artisan cannot reasonably be apprised of the metes and bounds of the claims. Furthermore, the purpose of the mutation of the cFRT chromosome (after it has been made) with regard to making the cFRT chromosome (the elected claimed method) is unclear, especially in light of the fact that the claimed method has been completed prior to the mutation of the cFRT. Applicant is reminded that the elected invention is a method of *making* the cFRT, and not a method of using the cFRT.

Regarding claims 17, 19 and 21, the phrase "including" is equivalent to the phrase "for example," which renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 18 recites the phrase "can be recovered" in the second line of the claim. This term is indefinite because it is unclear if the step is required to make the chromosome, due to the fact that the phrase "can be" is conditional language (for xample, under what conditions would you or would you not "recover"). Therefore, the metes and bounds are not defined because it is unclear if the method step is within the metes and bounds of the claim.

Claim 18 recites the phrase "related bioinformatic manipulation." This term is indefinite because it is unclear how a "bioinformatic manipulation" is determined to be "related" to the method of making a cFRT.

Claim 21 recites the phrase "further analyzed" in the second line of the claim. This term is indefinite because it is unclear what is encompassed by this "further analysis" (i.e., what step(s) should be performed), therefore the metes and bounds of the term are not defined.

Claim 26 recites the limitation "said FLP" in the penultimate line of the claim. There is insufficient antecedent basis for this limitation in the claim.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson, Ph.D.
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JAMES KETTER
PRIMARY EXAMINER